

Tumor Bed Implant Brachytherapy for Residual Carcinoma After Palliative Esophagectomy

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Twenty-six patients with esophageal carcinoma at stage pT4 underwent esophagectomy with lymph node dissection leaving part of the tumor in adjacent organs. Several plastic catheters were fixed to the tumor bed and led to the outside of the thorax for postoperative brachytherapy. Using these catheters, the patients underwent brachytherapy followed by external beam irradiation. The operative mortality rate was 11.5%. No serious complications resulting directly from the brachytherapy occurred. Recurrent disease was found in 17 patients, among whom only six had local recurrence. The median survival of the patients was 314 days, and the 5-year survival rate was 16.2%. Of the 10 patients at stage pT4N0, three survived more than three years after surgery. Tumor bed implant brachytherapy for residual tumor after esophagectomy is a safe and useful treatment strategy for patients with pT4 tumor, especially those without lymph node metastasis. © 1996 Wiley-Liss, Inc.

KEY WORDS: esophageal carcinoma, esophagectomy, lymphadenectomy, brachytherapy, radiotherapy

INTRODUCTION

The prognosis of patients with T4 carcinoma of the thoracic esophagus is generally pessimistic, except for patients who undergo radical surgery with combined resection of invaded adjacent organs [1-4]. Palliative esophagectomy may contribute to their survival to some extent [5-7]. After palliative esophagectomy, external beam irradiation is generally used as an additional treatment. However, most patients suffer tumor recurrence in adjacent organs sooner or later, despite postoperative radiotherapy. The tolerable dose of external beam irradiation for such patients is limited. With the aim of reducing the burden for patients after major surgery, to avoid a high-dose irradiation of the lung and spinal cord, which are the absolute dose-limiting organs, and to intensify the effect of postoperative radiotherapy by optimizing the radiation dose distribution, we carried out a tumor bed implant brachytherapy for the residual tumor in adjacent organs followed by external beam irradiation after esophagectomy. This paper assesses the results of the treatment and discusses its practical value.

PATIENTS AND METHODS

Between 1988 and 1994, 26 patients with thoracic esophageal carcinoma invasive to adjacent organs (pT4) underwent palliative esophagectomy with lymph node dissection by right thoractomy and laparotomy. The esophagectomies were performed leaving part of the tumor in adjacent organs (R2 esophagectomy according to the TNM classification [8]), because complete resection of the tumor combined with the invaded adjacent organ was judged to be impossible. The mediastinal and abdominal lymph nodes were dissected in 24 of the patients, as well as the cervical lymph nodes in 19. In patients who were suspected to have T4 tumor, radiologists were asked beforehand to wait ready to supply catheters and to instruct the surgeon about placing them in the best position for brachytherapy. Two to four plastic catheters, each

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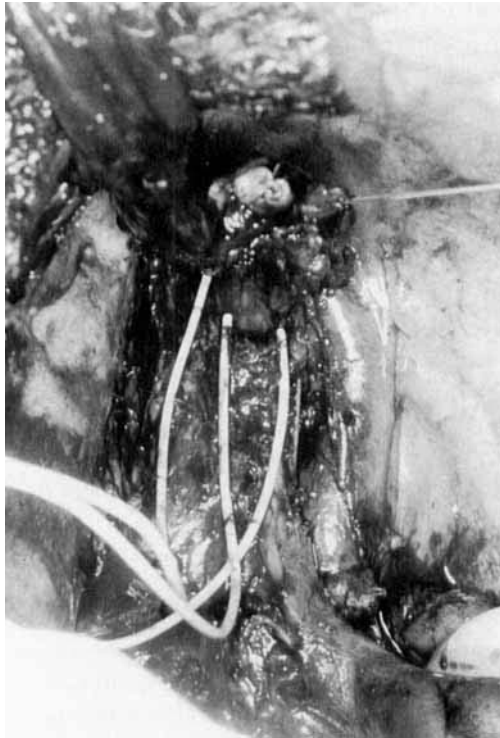


Fig. 1. The upper mediastinum during thoracotomy. Three plastic catheters for brachytherapy are placed behind the trachea.

with a sealed end, were placed on the tumor bed in the adjacent organ approximately one centimeter apart from each other, and fixed using two or three stitches of fine absorbable thread. When a large amount of tumor tissue or the ulcer bottom of a tumor was left in the wall of the adjacent organ, the catheters were placed after the tumor had been dissected as far as possible to reduce the tumor volume and clean the tumor surface. The catheters were led to the outside of the thorax through the intercostal space or to the neck via small stab wounds (Fig. 1).

Several days after surgery when the patients had recovered from postoperative crisis, thin ^{192}Ir wires were placed on the tumor bed through the catheter. The target dose of the brachytherapy in general was 20–30 Gy. Brachytherapy took 3–7 days, and delivered 4–76 Gy of radiation to each patient. Two patients received 70 Gy or more radiation by brachytherapy because they had undergone external beam irradiation before surgery in another hospital or had surgical complications. The catheters were immediately withdrawn when the brachytherapy was completed. Most of the patients, except for four who were in unstable condition after surgery or had undergone prior irradiation before surgery, underwent additional external beam X-ray therapy (30–60 Gy) several weeks after surgery. In most patients, except for some with many positive nodes, the radiation field was limited to the site of the residual tumor.

TABLE I. Characteristics of Patients With Residual Carcinoma After Palliative Esophagectomy

No. of patients	26
Age (mean \pm SD)	60.8 \pm 9.4 yr
Sex (male/female)	25/1
Tumor location [7]	
Upper thoracic esophagus	9
Middle thoracic esophagus	15
Lower thoracic esophagus	2
Preoperative TNM classification [7]	
T2/T3/T4	1/9/16
N0/N1	7/19
M0/M1 (LYM)	19/7
Gross tumor size (mean \pm SD)	6.9 \pm 1.8 cm
Histological classification [8]	
Squamous cell carcinoma	25
Adenosquamous carcinoma	1
Pathological TNM classification [7]	
pT4	26
pN0/pN1	10/16
pM0/pM1 (LYM)	17/9
Prior therapy	
Radiotherapy	1
Chemotherapy	1
Radiotherapy + chemotherapy	2

The patients' characteristics were adjusted and are shown in Table I. Not only esophagography and endoscopy, but also computed tomography (CT) scanning, cervical and abdominal ultrasonography, endoscopic ultrasonography, bronchoscopy, and in some cases magnetic resonance imaging (MRI) were used for preoperative staging. Ten of the 26 tumors had been diagnosed as not invading the adjacent organs before surgery, but were later during the operation found to have invaded. Seven patients had been diagnosed as having metastasis in the cervical and/or celiac lymph nodes. Histologically, two more patients were found to have metastasis in these nodes. Four patients who had undergone radiotherapy and/or chemotherapy in other hospitals were moved to our hospital before surgery, because the former hospitals had considered that surgery was not indicated.

The tumor stage was represented according to the 1987 TNM classification [8]. The WHO classification [9] was used for the histological classification of the tumors. The prognosis of the patients was investigated in December 1994. The survival rates were computed according to the life-table method of Cutlar and Ederar [10], including patients who had died of operative complications.

RESULTS

Although one of the catheters fell out just after surgery in two patients, brachytherapy was accomplished in these patients using the remaining catheters. In one patient, perforation of the membranous portion of the main bronchus where the catheters were implanted was noticed by routine bronchoscopy after surgery. However, it healed

TABLE II. Summary of Short-Term Results

Duration of operation (mean \pm SD)	523.5 \pm 62.2 min
Blood loss (mean \pm SD)	790.4 \pm 504.5 ml
Hospital stay (mean \pm SD)	101.2 \pm 40.0 day
Operative mortality rate	11.5%
Operative complications	
Anastomotic leakage	9
Recurrent nerve palsy	10
Pneumonia	4 (1 fatal)
Empyema	1 (fatal)
Nonocclusive mesenteric ischemia	1 (fatal)
No complication	10

spontaneously after removal of the catheter and caused no further complications. All of the patients lived for more than 30 days after surgery, although three of them died of operative complications after 30 days. The short-term results of this treatment are summarized in Table II. The hospital stay included that for preoperative examinations and for postoperative treatments. One patient had nonocclusive mesenteric ischemia after esophagectomy and died of liver failure 218 days after surgery despite emergency subtotal bowel resection. Another patient died of synpneumonic empyema 167 days after surgery. In some patients, the recurrent nerve was dissected along with the tumor because of tumor involvement. In the other patients, it was difficult to find and preserve the nerve because of massive tumors in the upper mediastinum. The mean (\pm SD) size of the resected tumor specimens was 6.9 \pm 1.8 cm.

The long-term results for each patient after these treatments are shown in Table III. Nine patients were classified as stage pM1 because of metastasis in the cervical and/or celiac lymph nodes. Recurrent disease was found in 17 patients; in six (35.3%) of these, the tumor recurred in adjacent organs in which part of the tumor had been left and irradiated after surgery. Control of the local tumor was not dependent on the dose of brachytherapy. Meanwhile, 11 patients had hematogenic or lymphogenic recurrence without local recurrence of the tumor.

Autopsy was performed on four patients, and two of them had no local recurrence histologically.

The median survival for all the patients was 314 days, and the cumulative 3- and 5-year survival rates after surgery were both 16.2%. Of the 26 patients, eight lived more than 365 days, among whom six patients are still alive at the time of writing. Seventeen patients died of recurrent disease, among whom one was a case of hospital death. Thus, including three patients who died of surgical complications, there were four hospital deaths. The other 22 patients obtained palliation and were able to return to a full diet. There were 10 patients at stage pN0 in this series, of whom five are still alive, three being without disease more than three years after surgery. The cumula-

tive 3- and 5-year survival rates for them were both 45.0%. All deaths were included in the survival calculation.

DISCUSSION

The role of surgery for patients with esophageal carcinoma at stage T4 is controversial, because for them the majority of esophagectomies remain palliative, and the survival rate after surgery is generally unfavorable. However, the number of patients with T4 tumor is not small, and they frequently undergo esophagectomy with palliative intent [6]. Moreover, we are often obliged to perform esophagectomy for a tumor at stage pT4, because preoperative diagnosis of tumor invasion to adjacent organs is often difficult or erroneous [4]. In our series, wall penetration by the tumor was underestimated before surgery in 10/26 (38.5%) patients, irrespective of diagnostic modality, and treatment decisions had to be made during surgery.

This tumor bed implant brachytherapy technique is considered to have added no further burden for the patients to the usual esophagectomy. The amount of operative blood loss seems reasonable for this kind of surgery. The operative mortality rate of 11.5% after palliative esophagectomy in our series also seems reasonable [5]. Serious complications resulting directly from the brachytherapy did not occur after surgery. In many patients at this stage, recurrent nerve palsy may become inevitable as the tumor progresses.

Although the optimum radiation dose for brachytherapy may be a matter of argument, the doses established in our series caused no serious complications. Whether or not local control was obtained did not depend on the dose of brachytherapy, at least within our established dose range. The local recurrence rate of 35.3% seems low in these patients with tumors at pT4 [11]. Autopsy showed that two of four patients had no tumor in the brachytherapy field. According to these results, our established radiotherapy using brachytherapy and external beam irradiation may be considered to have been suitable for control of locally advanced disease.

The prognosis of patients with esophageal tumor at stage T4 or pT4 is generally known to be very poor. However other than our report [1], there are no published survival rates for large numbers of patients with esophageal carcinoma at this stage. The reported 3-year survival rates for patients with tumors at stage T4 and pT4 in that series were 16.4% and 33.1%, respectively. The cumulative 3- and 5-year survival rates for the present series of patients were both 16.2%. Although the survival rates in the prior series seem better than in this series, the former included many patients whose tumors had been excised completely along with the esophagus. Moreover, the survival for the prior series was computed censoring all deaths except those due to cancer. The cumulative 3- and 5-year survival rates for this series of patients after censoring operative deaths and deaths due to other dis-

TABLE III. Tumor Status, Radiation Dose, and Long-Term Result for Each Patient

Patient no. age (yr), sex	Invaded adjacent organs	pNM factors	Radiation dose (Gy) Brachytherapy/External	Recurrence site	Outcome (days)
1 69 Male	Carotid	pN1M1	30/40	Lymph node	Died 300
2 69 Male	Trachea, bronchus	pN1M1	30/50	Bone, lymph node	Died 272
3 76 Male	Trachea, lung	pN0M0	30/50	—	Alive 2,435
4 52 Male	Aorta	pN1M0	30/50	Bone, other	Died 539
5 62 Male	Bronchus, lung, pericardium	pN1M0	30/—	Bone	Died 313
6 56 Male	Aorta	pN1M1	30/50	Lung	Died 355
7 58 Male	Bronchus	pN1M0	30/50	Skin	Died 155
8 49 Male	Trachea, aorta	pN1M0	76/—	Trachea, aorta	Died 167
9 70 Male	Bronchus, lung	pN0M0	70/—	—	Died 76
10 68 Male	Aorta	pN0M0	25/40	—	Alive 2,035
11 47 Male	Trachea	pN1M0	32/50	Trachea, bone	Died 160
12 45 Male	Pericardium	pN1M0	30/30	Pericardium	Died 930
13 79 Male	Bronchus	pN0M0	30/50	Lymph node	Died 712
14 58 Male	Trachea, aorta	pN0M0	30/50	Trachea, aorta, skin	Died 314
15 69 Male	Trachea, bronchus, aorta	pN1M1	30/—	Lung	Died 52
16 64 Male	Trachea, aorta	pN0M0	30/40	—	Alive 1,177
17 57 Female	Aorta	pN1M1	30/50	Skin, pleura	Died 200
18 58 Male	Trachea, aorta, spine	pN0M0	30/50	Trachea, aorta	Died 137
19 40 Male	Trachea, lung	pN1M1	30/30	Skin	Died 242
20 59 Male	Lung	pN1M1	20/30	—	Died 187
21 67 Male	Lung	pN0M0	20/50	Lung, pleura	Died 321
22 57 Male	Trachea, bronchus	pN1M1	4/44	—	Died 218
23 69 Male	Bronchus	pN1M1	24/60	Lung	Died 376
24 63 Male	Trachea, bronchus	pN0M0	25/40	—	Alive 391
25 63 Male	Trachea	pN0M0	25/50	—	Alive 314
26 57 Male	Bronchus	pN1M0	30/50	—	Alive 78

eases were both 20.1%. In any event, the 5-year survival rate for this series was nearly equal to that for all patients after esophagectomy reported in the world literature, where most of the patients would naturally have been at an earlier stage and undergone curative surgery [12].

Among 10 patients at stage pT4N0, five lived beyond 1 year, including three who lived more than three years. The 5-year survival rate of 45% for the patients at stage pT4N0 after this treatment seems favorable. When the patient with residual tumor in an adjacent organ has no lymph node metastasis, the prognosis after esophagectomy may be improved by postoperative tumor bed implant brachytherapy with external beam irradiation.

CONCLUSIONS

In patients with esophageal carcinoma at stage T4 N0M0, esophagectomy followed by postoperative tumor bed implant brachytherapy and external beam irradiation is recommended. It is desirable to carry out extended lymph node biopsy along with esophagectomy to estimate the prognosis of the patient.

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